A Measles Outbreak at a College with a Prematriculation Immunization Requirement

Bradley S. Hersh, MD, MPH, Lauri E. Markowitz, MD, Richard E. Hoffman, MD, MPH, Daniel R. Hoff, PA, Mary J. Doran, Jessica C. Fleishman, Stephen R. Preblud, MD, and Walter A. Orenstein, MD

ABSTRACT

Background. In early 1988 an outbreak of 84 measles cases occurred at a college in Colorado in which over 98 percent of students had documentation of adequate measles immunity (physician diagnosed measles, receipt of live measles vaccine on or after the first birthday, or serologic evidence of immunity) due to an immunization requirement in effect since 1986.

Methods. To examine potential risk factors for measles vaccine failure, we conducted a retrospective cohort study among students living in campus dormitories using student health service vaccination records.

Results. Overall, 70 (83 percent) cases had been vaccinated at ≥12 months of age. Students living in campus dormitories were at increased risk for measles compared to students living off-campus (RR = 3.0, 95% CI = 2.0, 4.7). Students vaccinated at 12–14 months of age were at increased risk compared to those vaccinated at ≥15 months (RR = 3.1, 95% CI = 1.7, 5.7). Time since vaccination was not a risk factor for vaccine failure. Measles vaccine effectiveness was calculated to be 94% (95% CI = 86, 98) for vaccination at ≥15 months.

Conclusions. As in secondary schools, measles outbreaks can occur among highly vaccinated college populations. Implementation of recent recommendations to require two doses of measles vaccine for college entrants should help reduce measles outbreaks in college populations. (*Am J Public Health* 1991;81:360–364)

Introduction

Since licensure of live measles vaccine in the United States in 1963, there has been a marked reduction of reported measles incidence. In 1978, the United States began an effort to eliminate indigenous measles. The elimination strategy called for achieving and maintaining high immunization levels, careful surveillance, and aggressive outbreak control. The high immunization levels were to be achieved using a single dose of measles vaccine.[1]

Although there has been a 98 to 99 percent reduction in the number of annual reported cases from the pre-vaccine era, measles outbreaks still occur. Two predominant patterns of measles transmission have been observed: outbreaks occurring in predominately unvaccinated inner-city preschool-age children, and outbreaks occurring in highly vaccinated secondary school and college populations.[2,3] While most outbreaks occur in secondary schools, cases from college campuses have accounted for between 1.5 percent and 19.8 percent of cases each year from 1980 to 1989 (Table 1).[4,5] In 1983, the record low year for reported measles cases, campus outbreaks and non-campus cases associated with these outbreaks accounted for 32.4 percent of total cases.[6]

There are several reasons why measles outbreaks may be likely to occur in colleges and universities. Some college-aged students may not have been vaccinated in the early years following licensure of measles vaccine; others may not have been appropriately vaccinated at school entry or thereafter. Data from serological surveys suggest that between 5 and 15 percent of college-aged individuals may be susceptible to measles.[7] The propensity for college students to congregate in large groups and their travel to areas where measles transmission is endemic may increase the potential for introduction and spread of measles virus on college campuses.

School immunization laws have been demonstrated to be an effective means of assuring high measles vaccination levels and preventing measles outbreaks among kindergarten through 12th grade children and adolescents.[8] The American College Health Association[9–11] and the Immunization Practices Advisory Committee of the US Public Health Service (ACIP)[12] have recommended that colleges and universities require students to present evidence of measles immunity as a condition for enrollment. In early 1988, a measles outbreak occurred at a college that had implemented such an immunization requirement. This outbreak provided an opportunity to investigate the occurrence of measles in a highly vaccinated college population and to examine potential risk factors for measles vaccine failure.

Address reprint requests to Bradley S. Hersh, MD, MPH, Division of HIV/AIDS, Center for Infectious Diseases, Centers for Disease Control, Atlanta, GA 30333. Ms. Fleishman is with the University of Colorado Health Sciences Center; Drs. Markowitz and Orenstein are also with the Division of Immunization at CDC; Dr. Preblud, now deceased, was also with that Division; Dr. Hoffman and Ms. Doran are with the Colorado Department of Health, Denver; Mr. Hoff is a Physician Assistant with the Student Health Service, Fort Lewis College, Durango, CO. This paper, submitted to the Journal February 26, 1990, was revised and accepted for publication August 13, 1990.

TABLE 1—Reported Measles Cases on US College Campuses, 1980–89

Year	Total US Cases	Campus Cases		No. of Colleges Reporting Cases
		No.	%	
1980	13,506	200	(1.5)	36
1981	3,124	101	(3.2)	19
1982	1,714	115	(6.7)	14
1983	1,497	296	(19.8)	19
1984	2,587	67	(2.6)	17
1985	2,822	354	(12.6)	26
1986	6,282	174	(2.8)	21
1987	3,655	141	(3.9)	22
1988	3,396	267	(7.9)	20
1989	18,193	1,643	(9.0)	93

Background

Fort Lewis College is a public four-year college in Durango, Colorado. There were 3,555 students registered at the time of the outbreak. Since September 1986, the college has required students to provide proof of immunity to measles, as well as to other vaccine-preventable diseases, before enrolling. Adequate measles immunity was considered documentation of physician-diagnosed measles, receipt of live measles vaccine on or after the first birthday, or serologic evidence of immunity. Prior to this outbreak almost 99 percent of the student population were in compliance with this requirement and had documentation on file at the student health center.

Methods

Case Definition and Case Ascertainment

A case of measles was defined as an illness that met the Centers for Disease Control clinical case definition[13] (generalized maculopapular rash ≥3 days duration, fever ≥101 F, if measured, and at least one of the following: cough, coryza, or conjunctivitis). A suspected case was any rash illness with fever; a confirmed case met the clinical case definition and was either serologically confirmed or epidemiologically linked to another confirmed or clinical case of measles. A case was considered to be serologically confirmed if there was a fourfold rise in titer between acute and convalescent specimens by the complement-fixation assay.

Students were informed about the outbreak by class announcements, articles in the student newspaper, and reports on the campus radio station. They were instructed to report to the student health service at the onset of any febrile or rash illness. A disease control specialist from the Colorado Department of Health investigated every suspected case.

Outbreak Control

On January 8, 1988, after the third clinical case of measles was reported at the college, a manual review of college immunization records was conducted. A total of 40 students were found without documentation of measles immunity. All but three of these students were promptly vaccinated. The students not vaccinated had medical exemptions to vaccination and were excluded from campus for the duration of the outbreak. On January 12, 1988, the Colorado Department of Health placed the campus under public health orders. All indoor sporting events and other indoor college activities on or away from campus were restricted to participants who could show proof of measles immunity. All Fort Lewis participants in intercollegiate activities were examined prior to an event for signs and symptoms of measles prodrome. Furthermore, no spectators were allowed to attend these events. In order to prevent further measles transmission, all suspected measles cases among Fort Lewis College students were isolated in special dormitory rooms located near the student health service.

Retrospective Cohort Study

To investigate risk factors for measles vaccine failure, we conducted a retrospective cohort study among all students living in campus dormitories. Vaccination histories were obtained from student health center vaccination records. Student variables collected include: name, sex, race, class, date of birth, and housing status. Students who had received measles vaccine less than 14 days prior to rash onset were considered to be unvaccinated. We investigated the following potential risk factors for vaccine failure: number of doses of measles vaccine received, age at vaccination, and time since vaccination. Since several investigations of recent measles outbreaks have found individuals vaccinated before 1980 to be at higher risk for measles than those vaccinated in 1980 or after,[14] we also evaluated year of vaccination.

Age at vaccination was defined as the number of months between the date of birth and the most recent vaccination date on the vaccination record. Time since vaccination was calculated as the number of years between the date of most recent vaccination and the beginning of the outbreak (January 1, 1988). The age-at-vaccination analysis was limited to single dose vaccinees who were vaccinated before 1980; the time-since-vaccination and year-of-vaccination analyses were limited to single dose vaccinees who were vaccinated at 15 months of age or older. Finally, in order to verify information contained in case vaccination records, efforts were made to contact health care providers who had administered the vaccine. A physician-verified vaccination record was defined as confirmation of at least month and year of vaccination.

Differences in attack rates among groups in the retrospective cohort study were measured using the chi-square and Fisher's exact tests. Measles vaccine effectiveness and 95 percent confidence intervals were calculated using the method described by Orenstein, et al.[15]

Results

Between December 15, 1987, and March 10, 1988, a total of 84 measles cases in five generations of measles transmission occurred among Fort Lewis College students (Figure 1). All cases satisfied the clinical case definition for measles. Of the total cases, 11 (13 percent) were serologically confirmed.

The index case was an 18-year-old female freshman from South Carolina who had been vaccinated against measles at 14 months of age. The source of her infection is unknown. Measles transmission from the index case to second generation campus cases occurred at the Durango airport. Further measles transmission occurred primarily in campus dining halls, in classrooms, and at several campus social events. There was no spread of measles to other schools despite 10 inter-collegiate indoor activities or games, and only five cases were reported among non-college

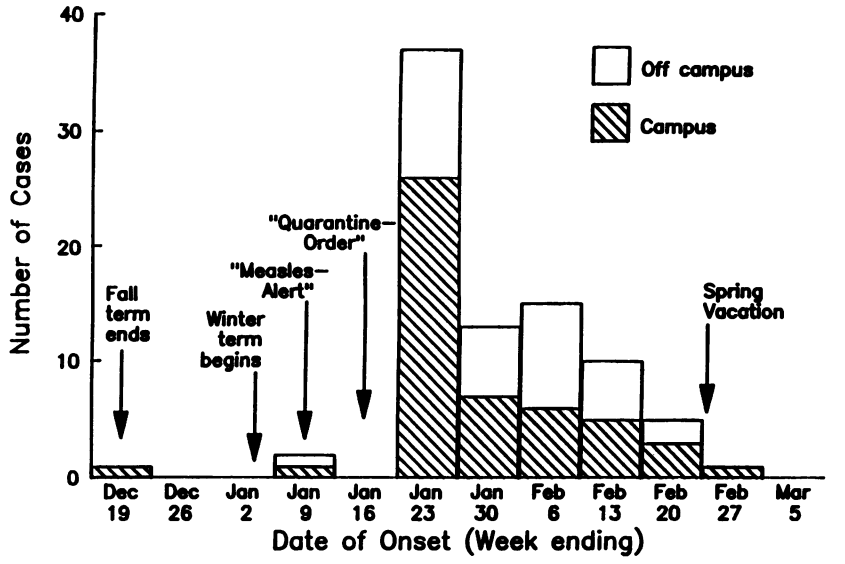

FIGURE 1—Reported Measles Cases by Week of Rash Onset, Fort Lewis College, December 1987–March 1988.

residents of Durango. Two of the non-college cases were directly linked to the index case.

Of the 84 cases, 70 (83 percent) occurred in individuals with evidence of measles vaccination at 12 months of age or older, including 20 (24 percent) vaccinated at 12 to 14 months of age. Of the 70 cases, vaccination histories (89 percent) were verified by the physician who had administered the vaccine. Five cases (6 percent) occurred in persons vaccinated before the first birthday, and 9 cases (11 percent) occurred in persons without documentation of measles vaccination. Of the cases in students without documentation of measles vaccination, vaccine was not routinely recommended for four (two born before 1957, two with a history of physician-diagnosed measles), and a fifth student had a religious exemption to vaccination.

Forty-six cases (55 percent) were freshmen, 46 (55 percent) were males, and 53 (63 percent) occurred in students living in campus dormitories. Seventy-five (89 percent) cases were White, seven (8 percent) were Native American, one case (1 percent) was Black, and one (1 percent) was Hispanic. Cases ranged in age from 17–32 years; 62 (74 percent) occurred in persons 18–20 years of age.

The overall attack rate among Fort Lewis College students was 2.4 percent. There were no differences in attack rates by race. Attack rates by housing status, sex, and class are summarized in Table 2. Students living in campus dormitories were at higher risk for measles than students living off-campus. When the analysis was limited to students living in campus dormitories, differences in attack rates by class are no longer observed.

In the retrospective cohort study among students living in campus dormitories, students without documentation of measles vaccination and those vaccinated before 12 months of age were at greater risk for measles than students vaccinated at 12 months of age or older (Table 3). No case of measles occurred in 46 students who had received two doses of measles vaccine after 12 months of age. Students vaccinated once at less than 12 months or at 12 to 14 months of age were at greater risk for measles than those vaccinated once at 15 months of age or greater. Although students vaccinated prior to 15 months of age were at increased risk for measles, these cases accounted for only 30 percent of the total cases. Students vaccinated before 1980 were not at significantly increased risk for measles compared with those vaccinated in 1980 or after. No trend for increasing attack rate with increasing time since vaccination was observed among students vaccinated once at 15 months of age or older (Figure 2).

The estimates of vaccine effectiveness among students living in campus dormitories was 80 percent (95 percent CI = 51–92 percent) for vaccination at 12 to 14 months of age and 94 percent (95 percent CI = 86–98 percent) for vaccination at 15 months or greater.

Discussion

The Fort Lewis College measles outbreak occurred in spite of virtually complete implementation of a prematriculation measles vaccination requirement. It was thus similar to outbreaks that have occurred in recent years among highly vaccinated junior and senior high school populations.[16–21] While the prematriculation requirement may have prevented a larger outbreak, it is apparent that measles outbreaks, such as the one described, can occur in highly vaccinated populations.

In this outbreak, living in campus dormitories was found to be a risk factor for acquiring measles. The relatively crowded living conditions and high contact rate among students in a college dormitory can facilitate measles virus transmission from infected to susceptible individuals.

Consistent with other investigations,[22] vaccination before the age of 15 months was found to be a risk factor for measles vaccine failure. The increased relative risk observed in persons vaccinated before 15 months of age has been attributed to the persistence of maternal antibody in infants, which interferes with live measles vaccine. Although age of vaccination was found to be a risk factor, 60 percent of cases occurred in students vaccinated at 15 months or older. As in other investigations,[17,19,21,23,24] there was no evidence in this outbreak that the risk for measles increases with time since vaccination.

We did not find evidence that vaccination prior to 1980 was a risk factor for measles in this outbreak. Other investigations, however, have found this to be a risk factor for measles vaccine failure.[14] Prior to the addition of an improved heat stabilizer to measles vaccine in 1979, individuals may have received a less effective vaccine, causing lower rates of seroconversion and an increased risk for measles. Alternatively, one may speculate that the finding of a lower risk for measles in individuals vaccinated since 1980 may be due to the possibility that some of these persons may have, in fact, been receiving a second dose of measles vaccine. Students may often find it easier to receive a second dose of measles vaccine than to obtain documentation of their initial measles vaccination.

The investigation of this outbreak found measles vaccine to be over 90 percent effective for vaccination at 15 months or greater. Other investigations have found similar results.[25] The occurrence of

TABLE 2—Risk Factors for Measles, Attack Rates by Student Characteristics, Fort Lewis College

Characteristic	Students	Cases	Attack Rate	Relative Risk	95% CI
Housing					
Dormitories	1,278	53	4.1%	3.0	(2.0–4.7)
Off-campus	2,277	31	1.4%	1.0	referent
Sex					
Male	1,922	46	2.4%	1.0	(0.7–1.6)
Female	1,633	38	2.3%	1.0	referent
Class					
Freshman	1,347	46	3.4%	4.3	(1.9–10.1)
Sophomore	842	19	2.3%	2.9	(1.2–7.2)
Junior	603	13	2.1%	2.7	(1.1–7.2)
Senior	763	6	0.8%	1.0	referent
Class*					
Freshman	759	34	4.5%	2.5	(0.3–17.7)
Sophomore	352	13	3.7%	2.0	(0.3–15.2)
Junior	112	5	4.5%	2.5	(0.3–20.5)
Senior	55	1	1.8%	1.0	referent

*Among students living in campus dormitories.

measles outbreaks in populations with high immunization levels suggests that the estimated 5 to 10 percent vaccine failure rate may still provide enough susceptibles to allow sustained transmission of a virus as communicable as measles in some settings, such as a college dormitory.

The two national advisory bodies for immunization policy, the Committee on Infectious Diseases of the American Academy of Pediatrics (Red Book Committee) and the ACIP, have recently considered the problem of measles outbreaks in highly vaccinated populations and have recommended the institution of a routine two-dose measles vaccination schedule.[26,27] Furthermore, both committees recommend that college students have, at the time of college entry, documentation of having received two doses of measles vaccine after the first birthday. The American College Health Association has endorsed this recommendation.[28] Prematriculation immunization requirements provide a mechanism for colleges and universities to ensure that students are in compliance with this new recommendation.

Whether a second dose of measles vaccine will significantly increase population measles immunity and decrease the risk of measles outbreaks is not conclusively known. However, this investigation and several others have found lower risks for measles in persons who received two doses of vaccine.[17,19,21,23] The power of these studies to detect statistically significant differences, however, was low due to the relatively small number of multiple dose vaccinees. Experience from the military suggests that a second dose of measles vaccine should be effective in preventing outbreaks.[29]

Measles elimination has proved more difficult than previously predicted.[30] A single dose strategy, while highly effective, has not been able to totally prevent measles outbreaks. The full implementation of a routine two-dose measles vaccination schedule, however, should help reduce measles outbreaks in highly vaccinated populations. □

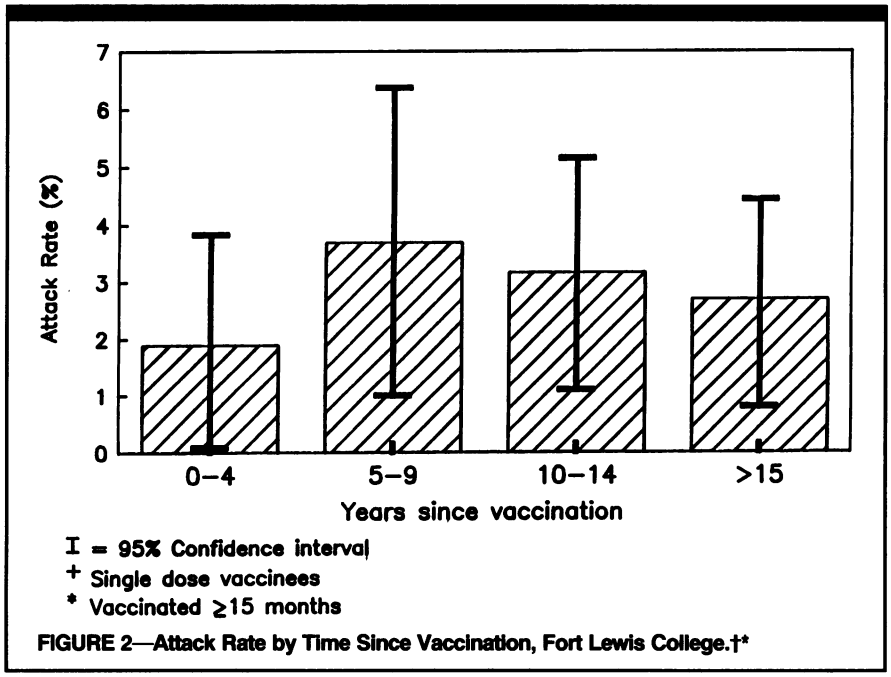

FIGURE 2—Attack Rate by Time Since Vaccination, Fort Lewis College.†*

Acknowledgments

The authors wish to acknowledge the assistance provided by the following individuals: Cameron Bordner, Edward Freienmuth, Michael Hocker, Sally Hudson, C. H. Reid, and Donald Whalen of Fort Lewis College; Deborah Banton, William Cornish, and Lynn Westberg of the San Juan Basin District Health Department; Judy Conner, Tim Englert, and Sallie Thoreson of the Colorado Department of Health; Nancy Adams, William Morris, Sonia Russell, Barry Sirotkin, John Stewart, Walter Williams, and Elizabeth Zell of the Centers for Disease Control.

References

1. Centers for Disease Control: Goal to eliminate measles from the United States. MMWR 1978; 27:391.
2. Frank JA, Orenstein WA, Bart KJ, *et al:* Major impediments to measles elimination: The modern epidemiology of an ancient disease. Am J Dis Child 1985; 139:881–888.
3. Markowitz LE, Preblud SR, Orenstein WA, *et al:* Patterns of transmission in measles outbreaks in the United States, 1985–1986. N Engl J Med 1989; 320:75–81.
4. Williams WW, Markowitz LE, Cochi SL, *et al:* Immunization in college health: The remaining tasks. J Am Coll Health 1987; 35:252–260.
5. Williams WW, Sosin, DM, Kaplan KM, *et al:* Vaccine-preventable diseases on college campuses: The emergence of mumps. J Am Coll Health 1989; 37:197–203.
6. Centers for Disease Control: Measles—United States, 1983. MMWR 1984; 33:105–108.
7. Amler RW, Kim-Farley RJ, Orenstein WA, *et al:* Measles on campus. J Am Coll Health 1983; 32:53–57.
8. Robbins KB, Brandling-Bennett D, Hinman AR: Low measles incidence: Association with enforcement of school immunization laws. Am J Public Health 1981; 71:270–274.
9. American College Health Association: Po-

TABLE 3—Risk Factors for Measles for Students Living in Campus Dormitories, Fort Lewis College

Characteristic	Students	Cases	Attack Rate	Relative Risk	95% CI
Doses					
0 doses	6	3	50.0%	13.1	(5.6–30.8)
1 dose (<12 mos)	52	5	9.6%	2.5	(1.1–6.1)
1 dose (≥12 mos)	1,156	44	3.8%	1.0	referent
2 doses (1 dose <12 mos and 1 dose ≥12 mos)	18	1	5.6%	1.5	(0.2–10.0)
2 doses (both doses ≥12 mos)	46	0	0.0%	0.0	(0.0–1.7)
Age at vaccination[ab]					
<12 mos	52	5	9.6%	3.0	(1.2–7.7)
12–14 mos	164	16	9.8%	3.1	(1.7–5.7)
≥15 mos	695	22	3.2%	1.0	referent
Year of vaccination[ac]					
<1980	695	22	3.2%	1.6	(0.6–3.8)
≥1980	297	6	2.0%	1.0	referent

[a]Single dose vaccinees
[b]Vaccinated before 1980
[c]Vaccinated ≥ 15 months

sition statement on immunization policy. J Am Coll Health 1983; 32:7–8.

10. Collins M, Bergy G, Bridwell MW: American College Health Association prematriculation immunization requirements. (editorial) J Am Coll Health 1984; 34:55.
11. Collins M, Smith DS: Prematriculation immunization requirements on college campuses: Current status. J Am Coll Health 1987; 35:247–251.
12. Centers for Disease Control: Rubella—United States, 1977–80. MMWR 1980; 29:378–380.
13. Centers for Disease Control: Classification of measles cases and categorization of measles elimination programs. MMWR 1983; 52:707–711.
14. Centers for Disease Control: Measles—United States, 1988. MMWR 1989; 38:601–605.
15. Orenstein WA, Bernier RH, Dondero TJ, *et al:* Field Evaluation of Vaccine Efficacy. Bulletin WHO 1985; 63:1055–1068.
16. Hull HF, Montes JM, Hays PC, *et al:* Risk factors for measles vaccine failures among immunized students. Pediatrics 1985; 76:518–523.
17. Nkowane BM, Bart SW, Orenstein WA, *et al:* Measles outbreak in a vaccinated school population: Epidemiology, chains of transmission, and the role of vaccine failures. Am J Public Health 1987; 77:434–438.
18. Gustafson TL, Lievens AW, Brunell PA, *et al:* Measles outbreak in a fully immunized secondary-school population. N Engl J Med 1987; 316:771–774.
19. Davis RM, Whitman ED, Orenstein WA, *et al:* A persistent outbreak of measles despite appropriate prevention and control measures. Am J Epidemiol 1987; 126:438–449.
20. Chen RT, Goldbaum GM, Wassilak SGF, *et al:* An explosive point-source measles outbreak in a highly immunized population: Modes of transmission and risk factors for disease. Am J Epidemiol 1989; 129:173–182.
21. Hutchins SS, Markowitz LE, Mead P, *et al:* A school-based measles outbreak: The effect of a selective revaccination policy and risk factors for vaccine failure. Am J Epidemiol 1990; 132:157–168.
22. Orenstein WA, Markowitz LE, Preblud SR, *et al:* Appropriate age for measles vaccination in the United States. Develop Biol Stand 1986; 65:13–21.
23. Shasby DM, Shope TC, Downs H, *et al:* Epidemic measles in a highly vaccinated population. N Engl J Med 1977; 296:585–589.
24. Marks JS, Halpin TJ, Orenstein WA: Measles vaccine efficacy in children previously vaccinated at 12 months of age. Pediatrics 1978; 62:955–960.
25. Preblud SR, Markowitz LE, Orenstein WA: Update on measles vaccine effectiveness. Proceedings of the 21st Immunization Conference, New Orleans, Louisiana 1987; 27–29.
26. American Academy of Pediatrics: Measles: Reassessment of the current immunization policy. AAP News 1989;(July):6–7.
27. Centers for Disease Control: Measles prevention: Recommendations of the immunization practices advisory committee. MMWR 1989; 38:S-9.
28. American College Health Association: Action (newsletter). 1989; 28:5.
29. Crawford GE, Gremillion DH: Epidemic measles and rubella in Air Force recruits: Impact of immunization. J Infect Dis 1981; 144:403–410.
30. Centers for Disease Control: Measles—United States, 1989 and first 20 weeks 1990. MMWR 1990; 39:353–355, 361–363.